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09/904,039	07/12/2001	Shoulian Dong	3218.2A	3123

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EXAMINER

KIM, YOUNG J

ART UNIT	PAPER NUMBER
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1637

19

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/904,039

Applicant(s)

DONG ET AL.

Examiner

Young J. Kim

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 05 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 38-53 and 57-173 is/are pending in the application.
- 4a) Of the above claim(s) 38 and 59-173 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 57 and 58 is/are allowed.
- 6) ☒ Claim(s) 39-53 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

This Office Action responds the Amendment received on August 8, 2003 (Paper No. 16).

#### ***Rejections – Withdrawn***

##### ***Double Patenting***

The rejection of claims 39-58 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 11-15, and 18-24 of U.S. Patent No. 6,361,947 B1, made in the Office Action mailed on May 5, 2003 is withdrawn in view of the terminal disclaimer filed with the Amendment received on August 8, 2003 and claim amendment to claim 39, and further in view of the cancellation of claims 54-56.

##### ***Claim Rejections - 35 USC § 102***

The rejection of claims 39, 44, 45, and 48-55 under 35 U.S.C. 102(e) as being anticipated by McCaskey et al. (U.S. Patent No. 6,100,030, issued August 8, 2000, priority January 10, 1997), made in the Office Action mailed on May 5, 2003 is withdrawn in view of the Amendment received on August 8, 2003, canceling claims 54 and 55, and amending claim 39.

##### ***Claim Rejections - 35 USC § 103***

The rejection of claims 40-43, 46, 47, and 56 under 35 U.S.C. 103(a) as being unpatentable over McCaskey et al. (U.S. Patent No. 6,100,030, issued August 8, 2000, priority January 10, 1997) in view of DeRisi et al. (Science, October 1997, vol. 278, pages 680-686), made in the Office Action mailed on May 5, 2003 is withdrawn in view of the Amendment

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received on August 8, 2003, canceling claim 56, and amending the independent claim 39 to which the instant claims depend from.

***New Rejection – Necessitated by Amendment***

Applicants' amendment to claim 39 necessitates the present rejection.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 39-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over McCaskey et al. (U.S. Patent No. 6,100,030, issued August 8, 2000, priority January 10, 1997) in view of DeRisi et al. (Science, October 1997, vol. 278, pages 680-686) and Moyer et al. (Applied and Environmental Microbiology, July 1996, vol. 62, no. 7, pages 2501-2507).

Claim 39 is drawn to a method of analyzing a first nucleic acid sample by fragmenting the first nucleic acid, ligating adaptor sequences to the resulting fragments, amplifying the ligated fragments and hybridizing the resulting amplified ligated fragments to a nucleic acid array and analyzing their hybridization pattern. Newly added limitation to this claim requires a computer to predict the fragmented nucleic acids, and provides a microarray comprising probes for these fragmented nucleic acids for the subsequent hybridization assay.

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Some embodiments are drawn to the percentage of second nucleic acid sample produced by the fragmentation method (claims 40-43).

Some embodiments are drawn to the first nucleic acid being a DNA (claim 44), genomic DNA (claim 45), cDNA (claim 46).

Some embodiments are drawn to the nature of the fragmentation produced by a restriction enzyme (claim 48), a type II's endonuclease (claim 49).

Some embodiments are drawn to the nature of the adaptor sequence (claim 50 and 51).

The method is also drawn to detecting a sequence variation in the nucleic acid (claim 52), wherein the variation is a single nucleotide polymorphism (SNP) (claim 53).

McCaskey Feazel et al., hereto referred to as '030 patent, disclose a method for detecting polymorphism (column 23, line 40; column 22, lines 33-37; **claim limitation 52 and 53**) in a nucleic acid sample by fragmenting genomic DNA (column 18, lines 20-21; **claim limitation 44 and 45**), ligating adaptor sequences to the resulting fragments (column 18, lines 24-25), wherein the adaptor sequences are complementary to the PCR primer sequences (column 18, lines 25-29 and 60-63; **claim limitation 50-51**), amplifying the adaptor ligated fragments and hybridizing them to a microarray comprising an array of nucleic acids which are complementary to the amplified, adaptor ligated fragments (column 23, lines 54-60). The method of the '030 patent employs a restriction endonuclease (column 18, line 21; **claim limitation 48 and 49**) for producing the nucleic acid fragments. The '030 patent discloses that any type of restriction endonuclease known in the art can be used to digest the DNA for its analysis (column 18, line 36-38).

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The '030 patent does not teach the amplified adaptor ligated nucleic acids (or second nucleic acids) comprising various percentage of the initial DNA population (claims 40-43), nor the DNA as being a cDNA produced from an RNA molecule (claim 46). The '030 patent also does not *explicitly* teach a method of determining the sequence of the probes of the microarray by a computer system, wherein the computer system is employed to predict the fragmented nucleic acid sequences.

Moyer et al. disclose a method of employing a computer simulation to predict fragmented nucleic acid sequences (page 2501, 2<sup>nd</sup> column).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of the '030 patent with the conventional knowledge in the art to arrive at the invention as claimed for the following reasons.

Although the '030 patent does not explicitly teach that the amplified, adaptor ligated nucleic acid (or second nucleic acids) comprises various percentage of the first nucleic acid population, the patent clearly demonstrates producing fragments which, by inherency, would have a varying degree of percentage of the first nucleic acid population.

Although the '030 patent does not use cDNAs produced from RNAs (claim limitation 46) for fragmentation, such knowledge, as demonstrated by DeRisi et al., is also within the purview of an ordinarily skilled artisan in the field of array hybridization:

“[v]irtually all differences in cell type of state are correlated with changes in the mRNA levels of many genes. This is fortuitous because the only specific reagent required to measure the abundance of the mRNA for a specific gene is a cDNA sequence.” (DeRisi at page 680, 1<sup>st</sup> column)

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The cDNA is disclosed as being derived from mRNA by reverse transcription process and hybridized to a DNA array (DeRisi at page 680, 3<sup>rd</sup> column).

Therefore, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in substituting the genomic DNA of '030 patent with the cDNA of DeRisi et al. because both types of DNAs were demonstrated to be hybridizable to DNA arrays. Furthermore, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in arriving at the claimed method which involves a computer to predict the fragmented sequence given the computer-simulation method disclosed by Moyer et al. with the motivation provided by the '030 patent, wherein it states:

“In one preferred embodiment, AFLP is used to identify differentially amplified nucleic acids, which are then converted into polynucleotide probes which map to polymorphisms. The differentially amplified AFLP DNAs are *converted into polynucleotide probes* by isolating individual polymorphic AFLP fragments from a mixture fragments in an AFLP amplification product, followed by using these isolated fragments (or clones or subclones thereof) as polynucleotide probes in *hybridization with immobilized DNA amplification mixtures (e.g., AFLP products)*.” (column 3, lines 27-36).

As the '030 patent motivates an ordinarily skilled artisan to employ the AFLP generated DNAs for array probes, the artisan would have had a reasonable expectation of success in taking this motivation with the computer simulation which predicts restriction fragments for the advantage of efficaciously, “detecting and differentiating...genes” (Moyer et al., page 2501, 2<sup>nd</sup> column and Abstract).

Therefore, the invention as claimed is obvious over the cited references.

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### *Conclusion*

Claims 39-53 are rejected.

Claims 57 and 58 are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

### *Inquiries*

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (703) 308-9348. The Examiner can normally be reached from 8:30 a.m. to 7:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (703)-308-3905. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). **NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be**

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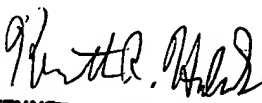
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sent to the Official Tech Center Fax number: (703) 872-9306. For Unofficial documents, faxes can be sent directly to the Examiner at (703) 746-3172. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Young J. Kim

10/16/03

  
KENNETH R. HORLICK, PH.D.  
PRIMARY EXAMINER

10/20/03